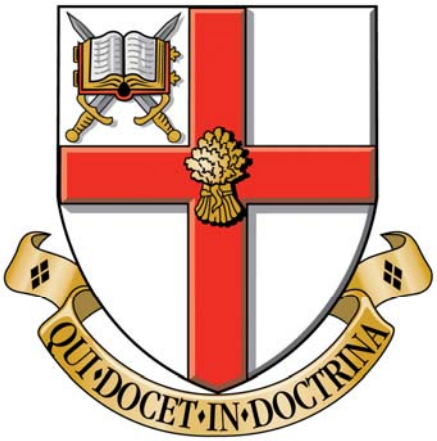


University of Chester

A Look at Life

A paper delivered at the conference:
The Interzone: communicating research enthusiasms across the disciplinary divide
Thursday 14th November 1996 at University College Chester

I get my title from one of the pleasures of my youth - time spent at the Odeon Cinema, Holloway where they used to show the newsreel 'Look at Life'. This was that cinema chain's equivalent of Pathe News - but without the poultry. This is really a serious point because I am concerned mainly with human beings and wish, in the main, to exclude other animals - even cockerels.

Let me begin more recently, however, with a reminiscence from a coffee break in the late 1980s when I was working in the Anatomy Department at University College Cardiff. The coffee break in that department was a very important occasion because at 11.00am everyday everything stopped and all the staff congregated upstairs in Room 408. It was on those occasions that a lot of discussion went on. Indeed, some people were only ever seen at coffee break. I remember overhearing one conversation where one anatomist asked another where he thought anatomy ended, that is, down to what level of structure one must go beyond which one would then be entering some other scientist's realm. The general conclusion to the discussion was that anatomy ended at the tissue level - beyond this one was entering the realm of the cell biologist and then that of the molecular biologist. These two anatomists did not really give a reasoned to sustain their ideas. Their lack of an argument stimulated me to address it instead. Was it all just a matter of tissue being the lowest level to which our scalpels could take us?

(The term anatomy, in the traditional sense, does, after all, mean 'cutting up'.)

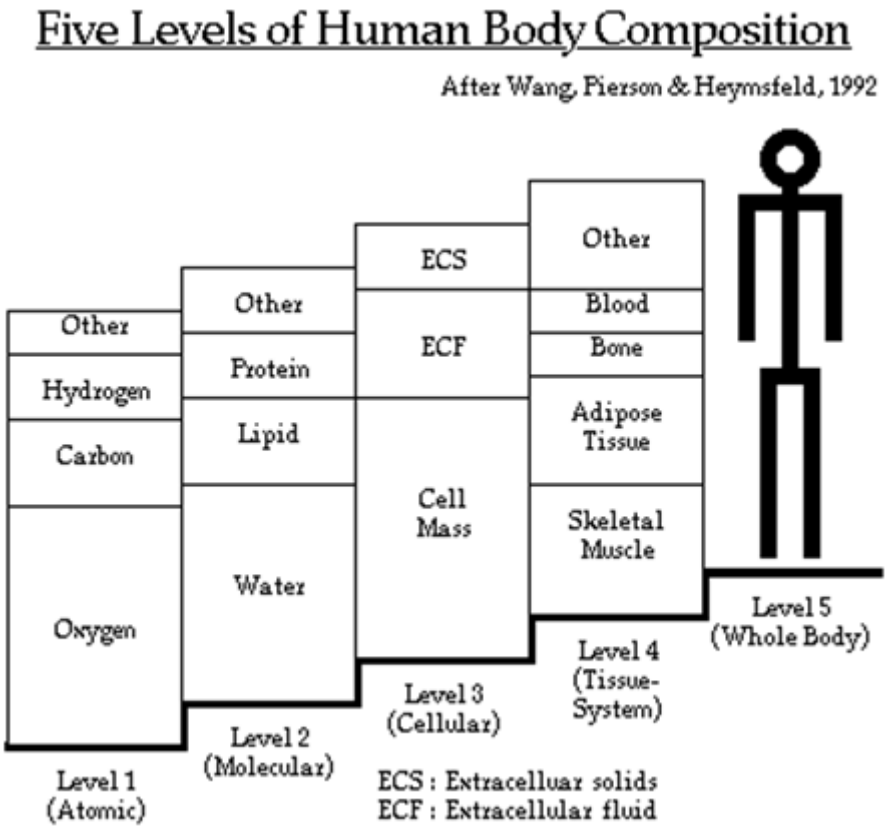
Not long after, I came across the concept displayed in this figure:

Levels of Structural Organization and Complexity within the Human Body

(From: McMurtrie and Rikel, 1991)

This is taken from an American book by somebody with the splendid name of Hogin MacMurtrie. It demonstrates the levels of structural organisation and complexity within the human body. It is something I like to use in teaching; it is a useful teaching and cogitating aid, one might say, because it is a useful way of dividing an integrated organism into *systems* which allows physiological study of organs; *tissues* which allow further anatomical study; *the cellular level* which allows cell study and *the chemical and molecular levels* which allow biochemical study. When I first came to Chester, I did a lot of reading on my evenings alone. One of the books I read was Watson's 'The Double Helix'. In it, I came across what I found to be a quite staggering comment - that when you go from the cellular to the molecular/chemical level, you move from the level of the living to the level of the non-living. We usually say to students that organisms as a whole are alive, that the systems are alive, that the

organs are alive, that the tissues are alive, that the cells are alive, but when you get below the cellular level then one cannot say that chemicals or molecules are 'alive'. Not even DNA can be said to be alive. The important words are 'living' versus 'non-living' - non-living, that is, as opposed to 'dead' which may be considered as being that which was once alive but now is not. These points I have used with various student groups to try to enhance their state of biological questioning. I later came across this version of, what we might now call 'The Levels Approach', used in an academic paper by Wang, Pierson and Helmsfield (1992) in The American Journal of Clinical Nutrition where the levels used were those of the whole person, tissues, cellular, molecular and the atomic.



The object of this division was to investigate human body constitution. Thus this levels approach has a practical benefit; it is something that is more than just a teaching or thinking aid - it is a research aid as well.

The idea of breaking people up into more manageable bits echoes what has been called Virchow's rationalist and reductionist view of life which saw living organisms as the "sum of the function of the individual organs ... the entire body is divided into a number of individual seats of life, the specific activities of which are dependent upon the nature of their elementary parts, therefore, in the last instance, upon the cells of which the entire body is composed."

Virchow had a view of life that saw living organisms to be the sum of the function of the individual organs; the entire body is divided into a number of individual seats of life, the specific activities of which are dependent upon the nature of their own elementary parts and thus, in the last instance, upon the cells of which the body is composed. That is something I want to query. It is worth remembering at this point that the type of answer one gets to a question is the product of the question itself. To quote Werner Heisenberg, the quantum physicist, in 'Physics and Philosophy': "What we observe is not nature itself, but nature exposed to our method of questioning." Or to take a less academically reputable source - a Chinese fortune cookie (to which I once saw reference made): "We do not see things the way they are; we see them the way we are." In many respects, this echoes something that the philosopher David Hume said, in 'An Inquiry Concerning Human Understanding', that "from causes which appear similar, we expect similar effects. This is the sum total of all our experimental conclusions."

There is a danger that when we get used to things, we cease to question them properly. If the answer to the questions depends on the type of questions posed, it must also be remembered that the questions posed depend on underlying assumptions implicit and otherwise.

"Consider the lilies in the fields ..." (Matthew 6:28) in particular, the number of their petals and the number of petals of other flowers.

PLANT	PETALS
Lilies	3
Buttercups	5
Delphiniums	8
Marigolds	13
Asters	21
Daisies	34, 55, 89

If you ask the average biologist what is the conventional view of how a flower gets its appropriate number of petals, the answer is that it is determined by the genetic code. In shorthand, they might say, "it's in the genes" - those molecules or chemicals that I described earlier as being 'non-living'. I want to suggest that this is, in fact, an over simplification; an over-simplistic approach and, in fact, when analysed it comes to little more than a statement of ignorance. It used to be in the past that when scientists or, as they were then called, natural philosophers, could not explain something, they would defer to divine providence. As a result of this, there came into being someone or something called "the god of the gaps". This god filled the gaps in our understanding. The problem for this god was that as the gaps got (or seemed to get) smaller, so did the god that plugged them. Now, people, instead of deferring to God, defer to genes instead. If we look carefully at these petal numbers carefully, we see something special but not immediately obvious. Going down the list we notice that each number is the sum of the two immediately before it. This is, in fact, what is called a Fibbonaci sequence after Leonardo of Pisa (aka Fibbonaci) (1170-

1250) who thought of this sequence in 1220 to support a mathematical model describing the way in which rabbit populations increased - which seemed to be a bit of a problem at that time. But if genes were really in control of these petal numbers, we might expect to get intermediate numbers of petals - which you do not. What we might say instead is that the product of the genes is constrained by certain external factors - here to do with the limited number of ways in which things can be packed together in a flower head. (For more on this, see recent works by Prof. Ian Stewart of Warwick University and Brian Goodwin, formerly of the Open University.) What's interesting about the Fibbonaci sequence is that it crops up in many places in nature where you might otherwise have expected genes to be at work and offering us a quick and easy 'It's the genes' (non-)answer. For example, the petals of a flower, the proportion of the bones of the arm and hand are in a Fibbonaci sequence or certainly in the underlying ratio to be found in that sequence. Interestingly, the golden section, that canvas size and proportion used in art, particularly in the ancient world, is based upon that ratio. There is something that we find appealing in that ratio. Whether it is because we have evolved in a world or universe within which it is a fundamental characteristic or for some other reason, nobody is sure.

This area of morphology is that of epigenetics. That is, not genetics *per se* but built upon it, that is, derived from genes or the products of genes. It is an area of study totally unheard of certainly by the general public but to those such as myself this is an area one finds to be much more interesting and important than mere genetics.

The present period of scientific development has been described as an age when most biologists seem to think that the only interesting thing about an animal is its DNA sequence. But if one was to ask

"Why are plants green?" the answer "Because their genes make them so" would be quite inaccurate. The greenness of plants is not under genetic control. The green comes because plants make chlorophyll and the greenness is a characteristic of that chemical. Whatever you do to a plant's genes, the chlorophyll it produces will always be green. This is dictated by the basic rules of physics and chemistry; by the way the universe is. The same argument can be applied, for example, to haemoglobin which is always going to be red. Similarly, one does not find blue-skinned or green-skinned people because the pigment we have in our skin has various reddish/brown properties specific to its chemistry. Although it is true to say that genes determine the production of these pigment chemicals, it is incorrect to say that genes determine colour. Clearly, one cannot simply state that every characteristic of a biological organism is reducible to its genes.

I would like to go on, therefore, to say a few things about the human genome project. Perhaps I should preface what I am going to say by pointing out that I am not really trying to have a dig at it but rather I want to bring up some points that have arisen in various things I have read lately. Firstly, although one never really gets to hear about it much in the media, there is a good deal of animosity in the scientific world to the human genome project. This is not so much over the way in which some scientists are using it as a means to bolster their own reputations and get themselves Nobel prizes nor about the way that some scientists are using it to make loads of money via the numerous companies being set up to cash in from it but rather over the falsity of the claims and promises that are being made and which are repeated blandly and almost blindly in the media every few weeks. Richard Lewontin is eloquent in his vitriol in his book 'The Doctrine of DNA'. There is a memorable section where he describes the project workers being 'disciples' of

this doctrine - here using that term to distinguish such scientists from those of a more independent mind. He states that "according to the vision of the project and its disciples we will locate on the human chromosome all the defective genes that plague us and then from the sequence of the DNA ... deduce the causal story of the disease and generate a therapy." The implication is that once the project has succeeded in its goal of sequencing the human genome, various therapies to sooth all our ills will become available almost immediately. Some question whether such therapies will ever be possible and go on to ask whether those involved in the human genome project are really concerned with health issues at all since so much emphasis is being given to mapping normal, healthy genes. Lewontin's questioning goes on using the illustration that the gene behind cystic fibrosis has been located, isolated and sequenced, that the protein coded by the gene has being deduced and been found to be very much like all other structural proteins in a cell such that no one knows what to do next. The Tay-Sachs mutation is even better understood. The enzyme has been found to have a quite simple, specific function and no one knows what sort of therapy to derive from this knowledge. I have to say that I sometimes find Lewontin's arguments to be not entirely convincing and there is always the nagging feeling that this human genome knowledge is going to be useful at some stage or other since it is only in retrospect that we can know whether anything proves useful; non-useful knowledge seems to disappear even though it continues to exist locked away inside some dusty tome somewhere. More importantly the problem for a growing number of scientists is the realisation that despite the various claims banded about, one cannot just look at the DNA and know what it is for. One cannot just look at DNA and say that is for the number of petals. As we have already noted, that can never be the case. Nor can one just look at DNA and say that such-and-such is the protein or amino acid

sequence that is going to made. Some code is known to be periphrastic which is a linguistic term for words such as, for example, the English word 'do'. This word came into the current English language from a 16th century Midlands dialect. Before it did, people would say "I know not" whereas we say "I do not know". If one looks closely at that sentence, the word 'do' does not do anything and does not mean anything. All it does is just fill in space. Some DNA code is just like that too. The trouble is you cannot tell which piece of DNA is just space filler and which is useful.

Consider the DNA bases: GTAATG. Usually the genetic code is divided into groups of three bases so that GTAATG, to the average biologist, codes for two amino-acids: the first valine, the other serine. However, sometimes it signals for a sort of protein cutting-up process instead whereas at other times it signals an editing process. At other times, it is just periphrastic – it does not do anything. One cannot tell from just looking at it what it is doing. Instead, the circumstances in which DNA exists are vitally important.

Consider this example.

(From: Kreel, 1971, p369)

This is a chest X-ray which, even to the untrained eye, looks as if there is something wrong. When we take another, more penetrating picture, two things are noticed. The first is that the spine should be straight but is scoliotic – it has got a side-to-side, S-shape curvature to it - also it is twisted and the patient's pelvis is actually pointing a different way to his chest. But what's under the shadow?

(From: Kreel, 1971, p369)

This is a teratoma. Tissue inappropriate to the location is being formed. We see that teeth are growing in the lungs! Ask an average biologist what makes teeth and they will say 'genes' and might suggest that 'tooth-making' genes have been turned on by accident. But one can also propose an epigenetic case that suggests that here there are cells growing abnormally which have the properties and potential to become teeth if exposed to external factors similar to those in the jaw. If 'tooth genes' were at work, they would need to be producing both tooth substance and tooth shape or else they could not be called 'tooth genes' legitimately. However, if that were the case, we might expect all the teeth to be correctly shaped and possibly arranged in the correct sequence from incisors to molars. In tooth formation, local conditions are known to play an important role: there is a famous experience that Steven Jay Gould relates in

his book 'Hen's Teeth' where the formation of teeth in the jaws of chickens can be induced by interfering with - not the genes - but the developing chicken jaw.

Lewontin says rather accusingly, "I sometimes suspect that the claimed significance of the genome sequencing project for human health is an elaborate cover story for an interest in the hermaneutics of biological scripture." What is driving the project, he suggests, is the desire of certain lobbyists to understand the genome for its own sake. That is not to say that there is anything necessarily wrong with that except, he argues, when it is dressed up as a health issue so as to get the status and the money which should be going to other health projects. As we have already noted, we will not necessarily get the therapies when the code is cracked. Furthermore, if genome workers are really concerned with curing people with genetic disorders - which as Lewontin notes are *relatively* few - then, he suggests, there should be much greater focusing on them rather than on the normal stuff.

Having said all of that, I am not really having a go at the human genome project but I would like to raise the issue about the way it has been blown up as 'health'. I am wholly in favour of mapping the gene and it is fascinating work although it is not my cup of tea but we need to be more clear about the ramifications of it. Also, another of the so-called dangers of this project that others are becoming concerned about is that the project may be leading a return of biological determinist. This time, however, it is coming via a back door entry into the collective consciousness disguised as a health issue. It has been said that a hen is an egg's way of making another egg. That is what biological determinist's argue. The argument then goes on in another guise to say that a human being is the gene's way of making more genes and that is certainly some of the

thinking of people on the project. It is the sort of mechanistic thinking that gives Richard Dawkins' 'The Selfish Gene' a bad name and it got sociobiology a bad name, too.

But we ought to remember:

Genes Яn't Us

or as Dobzhansky (1971) puts it more meaningfully:

"An all too often forgotten and yet most basic fact is that the genes do not determine traits or characters, but rather the ways in which the organism responds to the environment."

Although eggs and hens and humans and genes do interact and behave as Dawkins has described, such descriptions are also overlaid with interpretation which is succeeded (and in some minds superseded) by a whole set of ramifications over which such authors have any control.

I am not going through all the levels of organisation I showed you earlier but I would like to look, having queried what is going on at gene level, at the next layer up: the cells. Here I would like to quote Isaac Asimov not in his science fiction guise but from his encyclopaedic 'Guide to Science'. In it he says that "cells are the basic level of organisation of living things". Although cells have been seen and known about since the 17th century, it was not until the 19th century that the French physiologist, Rene Jochim Henri Dutrochet, proposed, in a largely overlooked report of 1824, that living things were composed of cells. It was not until the Germans Mathias Jakob Schleiden and Theodor Schwann independently in 1838 and 1839 also came out with this idea that people started thinking in terms of cells being the lowest level of life or smallest unit of life. It should not be overlooked that this concept arose at a

time when people did not know what was going on inside cells and neither did they know what the cells were doing in relation to each other and in relation to the other tissues or to the organism as a whole. So to suggest that a cell is the basic unit of life was, in fact, a very bold assumption.

Good definitions of life are very hard to come by and then to say that something is the lowest unit of it is again quite dodgy. The physicist, Doyne Farmer, has suggested life may be defined as having the following properties:

- Patterns in space and time
- Self reproduction
- Information storage of its self-representation (genes)
- Metabolism, to keep the pattern persisting
- Functional interactions - its does stuff
- Interdependence of parts, or the ability to die
- Stability under perturbations
- Ability to evolve

Exactly what each of these mean, I am not entirely clear but I include it simply to make people think. One problem is that a computer virus obeys all these traits whereas a biological virus does not and mules do not obey all these nor do blood cells. Gerald Joyce, of whom I know nothing except for this quote, suggests that "life is a self sustaining chemical system capable of undergoing Darwinian evolution." Now what I would suggest from such definitions is that one of the big problems of such definitions is that life is looked at as if it were a noun rather than a verb. A noun is to be described, whereas a verb is to be - whatever you do to a verb - conjugated, I suppose. Simple descriptions of 'life' do not seem to do it justice. Looking at figures and tables does not necessarily give any information.

Another definition of life is that it is a 'process'. That is getting a bit more active as it sees life as a behaviour that is not bound to a

specific material manifestation; it is something that is going on rather than something that is. One could draw from science fiction here because that definition allows for non-biological forms of life and it is interesting and perhaps fanciful to ponder that had the universe taken a slightly different course in its early stages, its basic physics and chemistry may have been different and assuming that life could have evolved under these different circumstances, its basic form would have been quite different but still definable as life!

Life on earth has been dated back to 3.85 billion years ago - at least, that is the earliest evidence for cells. However, it is only when we get to about 650 million years ago that we start seeing multi-cellular organisms, that is, organised structures of more than one cell. Here one should stop for a moment to realize that this means that, for 3.2 billion years, cells existed on their own. Indeed, they existed as such for a period nearly five times as long as the period during which multicellular systems have existed. 3.2 billion years is an incredibly long time which, when thought of in terms of life cycles - considering that cells these days have a habit of dividing every 20 minutes - means that that 3.2 billion years represents an inconceivable number of generations through which cells went before they started making organisms. The last 650 million years is just under 17% of the total time during which life has existed on Earth and yet in that relatively short time (with its relatively few number of generations), life has gone from cells to the complicated organisms that we and other organisms, plant and animal, are. So there is something that is literally incredible - in that I suspect we have not realized it fully yet - going on in that 17% of life's history.

It has been suggested that when cells became able to communicate with each other in some way, that was when life in its most complex form really began to take off. Thus, life is really a form of

communication. It has been suggested that groups of cells should be seen as a conference rather than a community. A conference is like those of us here today as opposed to those of us unable to attend. The latter may still be part of our college community but they are not part of this conference.

If we look at life on the cellular level, we have to conclude that it is a very throw-away phenomenon. This seems odd for something so important. If you think about frogs and fish, they produce millions of embryos to try to keep enough surviving offspring; humans are not immune from that. Males produce huge numbers of sperm in the hope that one will get through; females produce large quantities of eggs but only use one a month for a limited period. Also we find that only about 30% of human conceptions make it to birth and so there is a great 'throw away' of what appears to be less than viable. There is also the suggestion that 150 males are conceived per 100 females but that only 105 males are born per 100 females. Life seems to be militated against males. More recently, it has been suggested that it may be that some 300 males are conceived per 100 females. Furthermore, there is also the idea of the vanishing twin; that every conception starts off as if to produce twins but that usually one is lost. (It is a sobering thought because once upon a time there were two of me!)

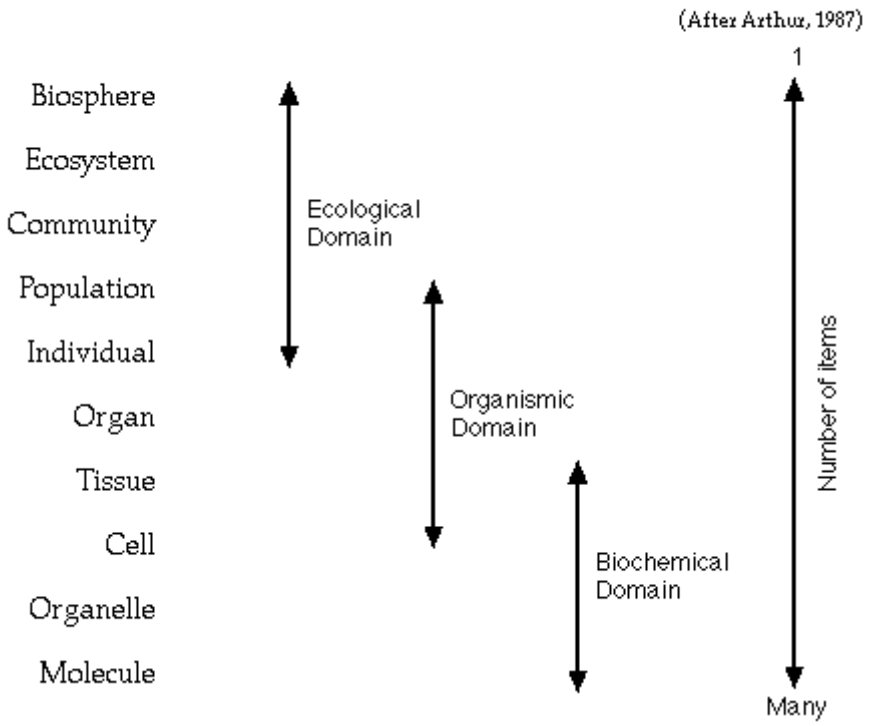
There appears to be a lot of cellular throw away going on at all stages in one's life history. In the human ear, there is a little bone called the stapes because it is stirrup-shaped and has a hole in it where a foot fits a stirrup. How does that hole get there? It is not the genes that make the hole; it is an artery. For a certain period *in utero*, an artery runs through the ear and the stapes forms around it. Later, that artery is lost (thrown away one might say) when its existence can no longer be sustained.

Diagram showing parts of external, middle and internal ear.

(From: Johnson & Kennedy, 1970, p217)

Another of the 'throw away' events in embryology - and one that is very important - is the loss of the bits between one's fingers and toes. The hands and feet start out as paddle-shaped structures within which the cartilage and then the bones of the fingers and toes form - but there are no spaces in between; these are formed when the cells between the digits die off. If these cells did not die we would have webbed fingers and toes. This 'throwing away' has, at a higher level, particular benefits.

I mentioned earlier the notion that a hen is an eggs way of making another egg or a human is a gene's way of making another gene. I also showed the diagram that I have used in the past to stimulate thinking about the levels of life. I am not entirely happy with it nowadays because I want to suggest that we might think in terms of genes being an environment's way of producing organisms suited to living in it. This idea arises from being able to use the 'Levels Approach' that we have applied to the human organism, more broadly and to see that it does not end with the organism.



This is the idea as used by Wallace Arthur (1987) where this approach goes much higher to include the whole biosphere. I am not qualified to use terms like Gaia which may be where we may be heading at this point and so I will not go any further.

As a group of workers, we are concerned, not only with the human as a biological organism but with community, with ecology and with our place in the wider world. What the important biological entity is in the final analysis, I do not wish to say. I suspect that this is another question that is the product of a way of seeing that limits our answers.

(Some) **References**

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